Non-Technical Abstract : Assessment of Retroviral-Mediated Incorporation of HSV Thymidine Kinase and Ganciclovir in Human Malignant Gliomas

Routine therapy of recurrent malignant gliomas involves obtaining several specimens by needle biopsy to verify the diagnosis and, within one week, a tumor resection.

Fifty microliters of vector-producing cells will be injected at each of three biopsy sites on day zero. Vector-producing cells generate replication-incompetent retrovirus vectors carrying the HSV-1 thymidine kinase gene. It is expected that the vectors will then infect nearby tumor cells and express thymidine kinase within the target cells. Two hours before tumor resection, the patient will receive ganciclovir at 5 mg/kg intravenously over one hour. This drug is nontoxic unless it is phosphorylated by HSV1-thymidine kinase, an enzyme not normally present in human tissues. Hence, only cells infected by the retroviral vector carrying the gene for this enzyme will be affected by the drug. It is expected that ganciclovir will be activated by the HSV1-thymidine kinase to a toxic product in tumor cells and that many of these cells will be killed.

The proposed protocol will treat three patients with 5×10^5 vector-producing cells at each of the three biopsy sites. Patients will be evaluated clinically for at least six weeks after tumor resection. Should there be no adverse effects, three additional patients will be treated with 2×10^6 vector-producing cells at the three biopsy sites. If no adverse effects are noted in this group, a final group of three patients will receive 5×10^6 at each biopsy site.